PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32752A	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/12593	International filing date *(day/month/year)* 11.11.2003	Priority date *(day/month/year)* 12.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/4184		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26.05.2004	23.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Albayrak, T Telephone No. +49 89 2399-7549

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12593

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-6 as originally filed

Claims, Numbers

1-13 as originally filed

Drawings, Sheets

1/14-14/14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-9

   because:

   ☒ the said international application, or the said claims Nos. 1-9 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-9
	No:	Claims	1-5, 10-13
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	10-13
	No:	Claims	-

2. Citations and explanations

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12593

see separate sheet

Re Item III

The subject-matter of claims 1-9 is related to subject-matter considered to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4) (a) (i) PCT).

Re Item V

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

D1:WO 01 10859 A (BAYER AG) 15 February 2001 (2001-02-15)
D2:RUFFI, P.: 'Nouvelles options thérapeutiques concernant le mésothéliome' REV. PNEUMOL. CLIN., vol. 58, no. 5 II, November 2002 (2002-11), pages 3S15-3S18, XP009027188
D3:MAUNG, K.: 'Novel drugs in development for malignant mesothelioma' CLINICAL LUNG CANCER, vol. 4, no. 3, November 2002 (2002-11), pages 146-148, XP001180104
D4: XP002258076

a) The subject-matter of the present application relates to the use of 4-pyridylmethyl-phthalazine derivatives for the treatment of mesothelioma.

b) The subject-matter of the present application is already known from D2-D3.

D2 and D3 disclose clinical studies on the treatment of mesothelioma with PTK787. The compound falls within the scope of the general formula 1 of claim 1 and is the preferred compound of the present application.
D4 discloses PTK787 for the inhibition of multiple myeloma cells.

Claim 10 is directed to a commercial package comprising a 4-pyridylmethyl-phthalazine derivative together with instructions for the use thereof in the treatment of mesothelioma. The feature "instructions for the use thereof in the treatment of mesothelioma" adds nothing to the pharmaceutical composition since it is directed to the use of the composition. The composition was claimed PER SE. Furthermore, this shall be regarded as a presentation of information which is contrary to Rule 67 (vi) PCT.

Therefore it appears, that the subject-matter of claims 1-5, 10-13 does not fulfill the criteria of Art. 33(2) PCT.

c) As for the inventive step the following comments apply:

D1 discloses compounds which fall within the general formula of claim 1 as well as the preferred compound of the present application for the treatment of conditions which are related to angiogenesis.
Mesothelioma is a form of cancer which is treatable by inhibiting certain tyrosine kinases or by inhibiting angiogenesis.
In the absence of any experimental or clinical data in the application no surprising/unexpected effect can be regarded. Therefore it appears, that the subject-matter of claims 6-9 cannot be regarded as fulfilling the criteria of Art. 33(3) PCT.